REMARKS

The specification has been amended to update the first line of the specification to recite the present status of U.S. Application Serial Number 09/799,937.

Applicants have added new claim 68.

New claim 68 has been added to encompass a specific embodiment of the invention. Support may be found in the specification, as published as U.S. Patent Application No. 2004/0166122, for example, at paragraphs [0051], [0061], and [0076].

No new matter has been added by these amendments.

After entry of these amendments, claims 10-19, 24-32, 47, 49-51, 53, 55-60, and 62-68 will be pending in the present application.

Applicants respectfully request entry of the foregoing amendments and consideration of the following remarks.

Interview Summary Record

Applicants wish to thank Supervisory Patent Examiner Bruce Campell and Examiner Benjamin Blumel for the courtesy of the telephonic interview conducted on September 18, 2007 with Applicant, Dr. Robert Evans, and Applicants' representative, Henry Wu.

During the interview, the references that are the basis for the rejection under 35 U.S.C. §103(a), i.e., Evans (Evans *et al.*, 2000, J. Pharm. Sci. 89:76-87) and Wu (U.S. Patent Application Publication No. 2002/0031527), were discussed. In particular, Applicants set forth reasons why (1) there is no basis for applying the teachings of Evans regarding EDTA/Ethanol in a plasmid formulation to an adenovirus formulation based on the differences between plasmid DNA and adenoviruses; and (2) Wu's teachings with respect to antioxidants must be taken into context of its teachings to minimize the effects of oxygen gas and provide no basis for using an inhibitor of free radical oxidation in an adenovirus formulation. The reasons are set forth in greater detail below.

Supervisory Primary Examiner Campell agreed to consider Applicants' arguments and conceded that a reference supporting the use of EDTA/Ethanol in adenovirus formulations needs to be found.

Specification

In response to the Examiner's request, Applicants have updated the first line of the specification to reflect the present status of U.S. Application Serial Number 09/799,937.

Double Patenting

Claims 10-18, 21, 24-32, 46-52, 55-60 and 62-67 were provisionally rejected over claims 1-5, 10 and 14 of copending Application No. 11/071,095.

Applicants note that the rejection is provisional and prosecution is ongoing. Applicants respectfully request that the provisional rejection be held in abeyance.

Claim Rejections – 35 U.S.C. § 103

Claims 10-19, 24-32, 47, 49-51, 53, 55-60 and 62-67 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wu in view of Evans. Applicants respectfully traverse.

The Examiner maintains that the present invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made because (1) one would have been motivated to modify the formulations taught by Wu given the suggestion that the antioxidants employed are not restricted to those specifically mentioned; and (2) there would have been a reasonable expectation of success given the knowledge that the combination of ethanol and EDTA stabilized DNA, as taught by Evans.

In response to Applicants' arguments set forth in the Amendment filed on March 16, 2007, the Examiner contends that (1) Wu teaches the use of antioxidants with multiple properties, including cleavage of di-sulfide bonds and reduction of hydroxyl radicals and that Wu disclosure of specific antioxidants are meant as examples, which are known in the art to reduce levels of free radicals; and (2) Evans teaches that adding EDTA/Ethanol stabilizes DNA based vaccines and thus one in the art would have been motivated to employ this combination to stabilize an adenovirus formulation in view of the teachings of Wu.

With respect to the Examiner's characterization of Evans, Applicants respectfully submit that there is no basis for applying the teachings of EDTA/Ethanol in a plasmid formulation to an adenovirus formulation. First, the skilled artisan would recognize that purified plasmid DNA is not similar to adenovirus either structurally, chemically or physically. These differences were discussed in detail in the Interview of September 18, 2007. Briefly, plasmid

DNA is supercoiled, circular DNA with no protein present, whereas adenovirus is approximately 85% protein and 15% DNA, with the linear DNA genome associated with DNA binding proteins and inside a protein capsid protected from the environment. Thus, adenovirus DNA is protected and inaccessible due to its location inside the virus capsid and because several adenovirus proteins (mostly polypeptide VII) complex tightly with the adenovirus DNA. Second, the skilled artisan would know that the available scientific literature on adenovirus stability suggested that the relevant degradation pathways for adenoviruses were likely to be capsid stability or aggregation, and made no references to free radical oxidation.

With respect to the Examiner's characterization of Wu, Applicants respectfully submit that Wu's teaching of antioxidants must be taken into the context of its teaching to minimize the effects of O_2 gas. Notably, both of the methods disclosed in Wu, i.e., (1) purging the lyophilization vessel with an inert gas; and (2) the use of antioxidants make it clear that the intended purpose is to remove oxygen gas, not to scavenge free radicals. See Wu, paragraph [0098]. Wu does not make any reference to free radical oxidation. Furthermore, there were no references that were available at that time of the present invention suggesting that free radical oxidation is a relevant degradation pathway for any adenovirus formulation. Thus, the skilled artisan would not have been motivated to add an inhibitor of free radical oxidation to liquid formulations of adenovirus because Wu does not teach or suggest inhibiting free radical oxidation and viruses were not known to degrade by free radical oxidation.

Finally, even assuming *arguendo* that an inhibitor of free radical oxidation could be used, the skilled artisan would not have added ethanol (alone or in combination with EDTA) to a solution about to be lyophilized because the ethanol would be removed by the lyophilization and have no effect. Wu only teaches the use of antioxidants for lyophilized adenovirus formulations. See Wu, paragraph [0098].

For the above reasons, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. 103.